=> d his

(FILE 'HOME' ENTERED AT 17:36:02 ON 30 DEC 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 17:36:28 ON 30 DEC 2003

```
L1         26000 S PARAMYXOVIURS OR PARAMYXOVIRIDAE OR MORBILLIVIRUS OR RUBULAVI
L2         21586 S (MUMPS OR PARAINFLUENZA OR SENDAI)(W)VIRUS
L3         16602 S (MEASLES OR RINDERPEST OR PHOCINE(W)DISTEMPER)(W)VIRUS
L4         47897 S (HUMAN OR BOVINE)(W)RESPIRATORY(W)SYNCYTIAL(W)VIRUS OR HSV OR
L5          2988 S (HUMAN OR BOVINE)(W)RESPIRATORY(W)SYNCYTIAL(W)VIRUS
L6         43783 S (SIMIAN OR NEWCASTLE(W)DISEASE)(W)VIRUS
L7         93899 S L1 OR L2 OR L3 OR L5 OR L6
L8           786 S (HETEROLOGOUS OR EXOGENOUS)(6A)(NUCLEIC(W)ACID OR POLYNUCLEOT
L9        851768 S MARKER
L10       852494 S L8 OR L9
L11         2236 S L7 AND L10
L12         6260 S (UPSTREAM OR'5')(5A)(NUCLEIC(W)ACID OR POLYNUCLEOTIDE OR VIRA
L13            1 S L11 AND L12
```

=> d bib ab l13

L13 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2001:816954 CAPLUS
DN 135:353772
TI Polynucleotides, and plasmid vectors containing said polynucleotides, and their use in recombinant production of adeno-associated virus virion
IN Colosi, Peter
PA Avigen, Inc., USA
SO PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001083797	A2	20011108	WO 2001-US40561	20010420
	WO 2001083797	A3	20030313		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2002052485	A1	20020502	US 2001-839583	20010420
PRAI	US 2000-200453P	P	20000428		

AB The invention provides nucleic acid mols. which can provide one or more accessory functions for supporting the prodn. of recombinant adeno-assocd. virus (rAAV) virion. The invention relates that said nucleic acid mols. can encode various proteins from adenovirus 2 or adenovirus 5, including the E4 ORF6, E2A 72-kilodalton, E1A, or E1B lacking an intact E1B55k proteins, or can encode the adenovirus virus-assocd. VA RNA gene. The invention also provides various an accessory function vector comprising said adenovirus nucleic acid mols. The invention further provides methods for producing rAAV virion which involves the use of an AAV plasmid vector, an AAV helper construct contg. the rep and cap genes, and said accessory function vector, which provides accessory functions needed in support of rAAV virion prodn. The invention relates that all three of these components are necessary for the recombinant prodn. of AAV. The invention also relates that in certain embodiments, the AAV helper construct may

include nucleic acid mols. for the accessory functions, as well as the AAV cap gene. Finally, the invention provides a system for prodn. of rAAV which uses the previous disclosed nucleic acid mols., as well as nucleic acid mols. encoding: (1) a SV40 large T antigen; (2) an Epstein-Barr virus nuclear antigen 1; (3) a SV40 origin of replication; (4) an Epstein-Barr virus latent origin of replication; (5) a selectable **marker**; (6) an ecdysone-inducible promoter; and (7) an ecdysone receptor subunit, wherein said nucleic acid mols. may be linked in various combinations in plasmid vectors. More specifically, the invention provided a rAAV producer cell line which had prodn. genes (such as E1A, E1B19K, EBNA1, VA RNA, E4ORF6, and ecdysone receptor subunit) and the AAV vector integrated into its genome in two different sites, and which also contained a plasmid contg. helper genes (E2A, rep, cap). Thus, overall the invention provides systems and methods for producing rAAV in which certain accessory and helper functions are located on a nucleic acid mol. that is maintained as an episome in the host cell. The invention discussed that the methods presented can be practiced to produce com. significant levels of rAAV particles without generating significant levels of infectious helper virus or other contaminating byproducts.

=>

=> d his

(FILE 'HOME' ENTERED AT 17:36:02 ON 30 DEC 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 17:36:28 ON 30 DEC 2003

```
L1         26000 S PARAMYXOVIURS OR PARAMYXOVIRIDAE OR MORBILLIVIRUS OR RUBULAVI
L2         21586 S (MUMPS OR PARAINFLUENZA OR SENDAI)(W)VIRUS
L3         16602 S (MEASLES OR RINDERPEST OR PHOCINE(W)DISTEMPER)(W)VIRUS
L4         47897 S (HUMAN OR BOVINE)(W)RESPIRATORY(W)SYNCYTIAL(W)VIRUS OR HSV OR
L5          2988 S (HUMAN OR BOVINE)(W)RESPIRATORY(W)SYNCYTIAL(W)VIRUS
L6         43783 S (SIMIAN OR NEWCASTLE(W)DISEASE)(W)VIRUS
L7         93899 S L1 OR L2 OR L3 OR L5 OR L6
L8           786 S (HETEROLOGOUS OR EXOGENOUS)(6A)(NUCLEIC(W)ACID OR POLYNUCLEOT
L9        851768 S MARKER
L10       852494 S L8 OR L9
L11         2236 S L7 AND L10
L12         6260 S (UPSTREAM OR'5')(5A)(NUCLEIC(W)ACID OR POLYNUCLEOTIDE OR VIRA
L13            1 S L11 AND L12
L14          932 S (MONITOR? OR REGULAT? OR MEASUR?)(5A)GENE(W)EXPRESS?(5A)(VIRA
L15            4 S L11 AND L14
L16            1 DUP REM L15 (3 DUPLICATES REMOVED)
```

=> d bib ab l16

L16 ANSWER 1 OF 1 MEDLINE on STN DUPLICATE 1
AN 93187597 MEDLINE
DN 93187597 PubMed ID: 8383171
TI Epstein-Barr virus (EBV) nuclear antigen 6 induces expression of the EBV latent membrane protein and an activated phenotype in Raji cells.
AU Allday M J; Crawford D H; Thomas J A
CS Department of Clinical Sciences, London School of Hygiene and Tropical Medicine, U.K.
SO JOURNAL OF GENERAL VIROLOGY, (1993 Mar) 74 (Pt 3) 361-9.
Journal code: 0077340. ISSN: 0022-1317.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199304
ED Entered STN: 19930416
Last Updated on STN: 19970203
Entered Medline: 19930402
AB Epstein-Barr virus (EBV) nuclear antigen (EBNA) 6 (also known as 3c) is a latent nuclear protein with an M(r) of about 160K which is invariably expressed in EBV-immortalized B cells. It includes a putative basic leucine zipper domain; as such it is a good candidate for a **regulator** of **viral gene expression**.
More than 75% of the EBNA 6 coding sequence is deleted from viral genomes carried in the Burkitt's lymphoma (BL) tumour-derived cell line, Raji. Thus although Raji cells express normal levels of the remaining five EBNAs and low levels of latent membrane protein (LMP), EBNA 6 protein is completely absent. In this study we have established Raji clones stably expressing EBNA 6 after cotransfection of an EBNA 6 gene under the control of the **simian virus** 40 early promoter with a selectable **marker**. Analysis of these clones has revealed that EBNA 6 induces a significant increase in the expression of LMP. In addition the cells have undergone a number of morphological and phenotypic changes consistent with blast-activation of normal B lymphocytes. The Raji cells expressing EBNA 6 show ruffling of the cell membrane and the development of a polarity defined by multiple villous ('spiky') projections at one end of the cell. This morphological change is associated with a dramatic increase in the expression of the cytoskeletal

protein, vimentin. The EBV-associated B cell activation **marker** CD23 (blast 2) is induced to high levels although other activation **markers** such as CD30 and CD39 are unaffected. All these changes appear to be independent of the precise levels of EBNA 6 protein expressed. EBNA 2 has been shown previously to trans-activate the LMP gene and in the control Raji cells, EBNA 6-positive Raji cells and in B lymphoblastoid cells similar levels of EBNA 2 are expressed. Our findings are therefore most consistent with a model in which EBNA 6 either augments or complements the action of EBNA 2 in the induction of LMP and the cascade of gene expression which leads to B cell activation and immortalization by EBV.

=>

=> d his

(FILE 'HOME' ENTERED AT 19:13:13 ON 30 DEC 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, SCISEARCH' ENTERED AT 19:13:34 ON 30 DEC 2003

L1 185 S GRADIENT(3A)GENE(3A)EXPRESS?
L2 32691 S PARAMYXOVIRIDAE OR PARAMYXOVIRUS OR MORBILLIVIRUS OR RUBULAVI
L3 2 S L1 AND L2
L4 2 DUP REM L3 (0 DUPLICATES REMOVED)
L5 162297 S MEASLES(W)VIRUS OR MV
L6 0 S L1 AND L5

=> d bib ab 1-2 l3

L3 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2003 ACS on STN
AN 2002:721115 CAPLUS
DN 137:258459
TI Positional effect of transgene insertion on expression level in **Paramyxovirus** vectors
IN Tokusumi, Takeshi; Iida, Akihiro; Hasegawa, Mamoru
PA Dinabeck Laboratory K. K., Japan
SO Jpn. Kokai Tokkyo Koho, 27 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 2002272465	A2	20020924	JP 2001-145935	20010516
PRAI	JP 2000-152726	A	20000518		
	CA 2000-2322057	A	20001027		

AB Virus vectors contg. a transgene placed downstream of viral protein coding genes comprising a **Paramyxovirus**, and use in regulating expression level of transgene, are disclosed. Sendai virus (SeV) is an enveloped virus with a nonsegmented neg. strand RNA genome. The recovery of infectious virus from cDNA and generation of recombinant SeV carrying a foreign gene at the promoter proximal position has been demonstrated. In this study, we constructed a series of recombinant SeVs carrying a reporter human secreted alk. phosphatase (SEAP) gene at each viral gene junction or the 5' distal end in order to measure the expression level of the foreign gene. We demonstrated that there was a **gradient** in the reporter **gene expression** level that depended on location, due to the polarity of transcription. Insertion of the transgene on the upstream side (3' of - strand), i.e., upstream of NP gene or between NP gene and P gene, was correlated with higher expression level. Transgene insertion on the downstream side (5' of - strand), i.e., downstream of L gene or between HN gene and L gene, on the other hand, was correlated with lower expression level. In contrast, the growth and final titers of these recombinant viruses showed an opposite **gradient** to the foreign **gene expression** level. This suggests the potential for matching therapeutic gene expression level to individual therapy programs by changing the position of the foreign gene when SeVs are used as vectors for human gene therapy.

L3 ANSWER 2 OF 2 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
AN 2002:452291 BIOSIS
DN PREV200200452291
TI Recombinant Sendai viruses expressing different levels of a foreign reporter gene.
AU Tokusumi, Tsuyoshi; Iida, Akihiro [Reprint author]; Hirata, Takahiro; Kato, Atsushi; Nagai, Yoshiyuki; Hasegawa, Mamoru
CS DNAVEC Research Inc., Tsukuba-shi, Ibaraki, 305-0856, Japan

iida@dnavec.co.jp
SO Virus Research, (June, 2002) Vol. 86, No. 1-2, pp. 33-38. print.
CODEN: VIREDF. ISSN: 0168-1702.
DT Article
LA English
ED Entered STN: 21 Aug 2002
Last Updated on STN: 21 Aug 2002
AB Sendai virus (SeV) is an enveloped virus with a nonsegmented negative strand RNA genome. The recovery of infectious virus from cDNA and generation of recombinant SeV carrying a foreign gene at the promoter proximal position has been demonstrated. In this study, we constructed a series of recombinant SeVs carrying a reporter human secreted alkaline phosphatase (SEAP) gene at each viral gene junction or the 5' distal end in order to measure the expression level of the foreign gene. We demonstrated that there was a **gradient** in the reporter **gene expression** level that depended on location, due to the polarity of transcription. In contrast, the growth and final titers of these recombinant viruses showed an opposite **gradient** to the foreign **gene expression** level. This suggests the potential for matching therapeutic gene expression level to individual therapy programs by changing the position of the foreign gene when SeVs are used as vectors for human gene therapy.

=>